
GABA progenitors grafted into the adult epileptic brain control seizures and abnormal behavior.

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Public Summary:

Impaired human nerve cells have been implicated in neurologic diseases, such as epilepsy. Healthy neural stem and progenitor cells can be used to create populations of interneuron progenitors for use as cell therapies. In this paper we report that transplantation and retention of healthy interneuron progenitor cells into the brains of epileptic mice greatly reduces the occurrence of seizures, corrects behavioral defects in spatial learning, and diminishes the hyperactive and aggressive responses to handling. Transplanted interneuron progenitors successfully migrated up to 1,500 mm away from the point of injection. After transplantation, interneuron progenitors matured and were found to express genetic and protein markers consistent with that of healthy mature interneurons. Our research demonstrates the ability of a cell based therapy to treat epileptic symptoms. This potential cell-based therapy is significant because current epilepsy drug treatments do not benefit all patients, the drugs can have significant negative side effects, and the drugs require regular dosing.

Scientific Abstract:

Impaired GABA-mediated neurotransmission has been implicated in many neurologic diseases, including epilepsy, intellectual disability and psychiatric disorders. We found that inhibitory neuron transplantation into the hippocampus of adult mice with confirmed epilepsy at the time of grafting markedly reduced the occurrence of electrographic seizures and restored behavioral deficits in spatial learning, hyperactivity and the aggressive response to handling. In the recipient brain, GABA progenitors migrated up to 1,500 mum from the injection site, expressed genes and proteins characteristic for interneurons, differentiated into functional inhibitory neurons and received excitatory synaptic input. In contrast with hippocampus, cell grafts into basolateral amygdala rescued the hyperactivity deficit, but did not alter seizure activity or other abnormal behaviors. Our results highlight a critical role for interneurons in epilepsy and suggest that interneuron cell transplantation is a powerful approach to halting seizures and rescuing accompanying deficits in severely epileptic mice.

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